

employment before the true nature of their disability is apparent.

Venereal Diseases.—There have only been three cases of acute gonorrhea for which employment was refused. One instance of rejection for a primary luetic lesion is recorded.

A study of the laboratory records for the past eleven months reveals positive Kahn blood tests averaging 0.97 per cent to 1.4 per cent for males, and 0.4 per cent to 2.4 per cent for females. For all colored individuals the percentage range was from 8 per cent to 19.0 per cent. The mean average for white males was .99 per cent, white females 1.6 per cent, and all colored people 11.56 per cent. The mean average of positive urinary albumin was .02, per cent and glycosuria from all causes .01 per cent.

Blood Dyscrasias.—A comparative survey of hemoglobin determinations for over one thousand applicants was made for the purpose of ascertaining if there was a lower average for Southern California residents. All ages and both sexes were considered. The only factor used was whether the individual had lived in California for more or less than one year. Those individuals having less than one year's residence were charted as to geographic origin. Thirty-nine States, representing all major sections of the United States, Canada, and Hawaii, are represented.

The Sahli method of hemoglobin determination was used.

The mean average of hemoglobin per cent for residents of California for over one year was 90.01 per cent and for those who have resided in the State less than one year, 91.4 per cent. The mean average for States in the deep South was 85.02 per cent, and for the northern states and Canada was 93.03 per cent. Hemoglobin determinations of 100 per cent were comparatively rare in this series.

Numerous instances of secondary anemia were found. There were three rejections for leukemia and two for pernicious anemia.

Chest X-Rays.—This is a subject for a separate report, and space in this article will only allow mention of some of the highlights.

Of the several thousand chest x-rays taken during 1942, the percentage of rejections for abnormal roentgenographic conditions was .018 per cent. There were .01 per cent of applicants who were employed with certain qualifications and who are rechecked at specified intervals.

The majority of the individuals rejected revealed evidence of pulmonary tuberculosis without calcific changes. The incidence of pulmonary fibrosis of a moderate to severe degree, where the second and third zones were particularly involved, was so frequent that 80 per cent is a fair estimate. In the first six months of 1942, over 22 per cent of chest plates revealed evidence of healed pulmonary tuberculosis, while the last six months revealed 48 per cent. This later period had over twice as many persons represented. This represents the period

of greatest influx from other areas. These individuals, for the most part, also represent the lower income groups from other states.

There have been four cases of active pulmonary tuberculosis hospitalized in the past six months. Time will tell the rest of this story. We have no record of the percentage of positive cases in the group rejected.

Under the part-time employment plan, high school students are being employed. There have been several hundred of these 'teen-age individuals put to work. In this group, one would expect to find the largest group of normal plates. The majority of the plates taken so far reveal the picture of heavy peribronchial infiltration with numerous instances of calcific changes. More study is being accorded this subject.

Numerous anomalies have been noted in these routine plates. There were thirty-three instances of unilateral, and twenty-four instances of bilateral cervical ribs recorded in 16,500 plates. Several times diaphragmatic hernia, eventration of the diaphragm, and mediastinal neoplasms have been found. Bronchiectasis and bullous emphysema have been noted.

There is one case of carcinoma of the lung which occurred after the individual was employed, which was followed to a lethal termination.

IN CONCLUSION

Industrial organizations today are facing an increasingly grave situation with reference to potential illness. The medical organization of the whole community must realize their responsibility in this task. Upon them, to an increasingly greater degree, will fall the burden of helping keep workers on the job and to lessen the hours of lost production. We shall do our share toward this end, but we who are dealing directly with the problem recognize the need for the fullest coöperation of the entire medical fraternity.

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CHEMOTHERAPY: ITS RÔLE IN TRAUMATIC SURGERY*

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THE value placed upon chemotherapeutic agents by the medical profession in general, and by the habitually skeptical surgeons in particular, has been stepped up to a high intensity in the past few years; in fact, an intensity it had not experienced since the days of Galen. There are many reasons why it should be so highly regarded, and even some of our notions about "surgical principles" will have to be revised. However, there is still plenty of

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opportunity for the exercise of good judgment and common sense.

SULFONAMIDE GROUP

The use of the sulfonamide group of drugs for topical administration in surgery got off to a slow start due to the poor results experienced in treating walled-off pyogenic infections. Although it is not entirely understood, it seems that the mode of action of the sulfonamide group is to render the various tissue fluids unfavorable as a medium for supporting the active multiplication of susceptible bacteria. To obtain this effect they must be in a sufficiently high concentration, and as they are relatively insoluble substances special conditions for their action must exist. In addition to the difficulty of insolubility there can be added the facts that the substances are broken down to form acetanilid in the tissues, and a certain proportion of the drug is bound to protein in such a way as to render it inert as a bacteriostatic factor. Of the various products now commonly in use, sulfanilamide is more soluble and less likely to combine with protein. In a bulletin issued in April, 1942, by the Bureau of Medicine and Surgery of the Navy Department it is recommended that only crystalline sulfanilamide be used for topical administration, and that sulfapyridine, sulfathiazole, and the other members of the group, be used by the oral and parenteral routes. One of the chief reasons for avoiding the implantation of sulfathiazole into wounds is the tendency of the particles to coalesce and form a foreign body. Since sulfathiazole has a particular effectiveness against certain organisms, notably staphylococcus, it is especially desirable that it can be used, and the objection to its "caking" will probably now be overcome by the use of the new microcrystalline sulfathiazole, which is available as powder and as a 10 per cent aqueous isotonic suspension. So far this substance is limited to investigational use. It has been our practice at the Naval Hospital at Mare Island to use a fifty-fifty mixture of sulfanilamide and sulfathiazole in its original form, and to attempt to overcome the difficulty of its acting as a foreign body by carefully spreading the material over the surface of the wound with the gloved finger in order to make a thin layer of the suspension against the wound edges.

Before making such an application it is important to do either a debridement of the wound or an entirely different procedure, complete wound excision. Since many of the wounds successfully treated with sulfonamide drugs are open infected wounds, often involving large areas, it is necessary to do frequent debridements. This means the removal of sloughs, coagulated exudate, dried pus, and the remains of tan. This can be accomplished by saline baths, by gentle mechanical removal, or by the application of starchy or gelatinous dressings to soften and facilitate the removal of such material. After this is done, the surface to be treated is lightly "frosted" with the crystalline material, either from a shaker container or by means of a powder blower. As the drug acts by going

into solution in the media in which the organisms grow, it is necessary that the wound be kept moist, while at the same time avoiding excessive moisture which would wash away the sulfonamide. One way of doing this is to overlay the wound with strips of gauze which have been impregnated with an ointment, and thereby cut down evaporation and prevent drying and crusting, or to spray the wound with a combination of waxes and oils kept above its melting point in a "flit gun." Such a combination of paraffine, petrolatum, and liquid petrolatum, together with cod-liver oil, essential aromatic oils, and containing some sulfanilamide powder in suspension, has been used with success by naval surgeons in the treatment of the extensive burns sustained at Pearl Harbor on December 7, 1941. It was a natural step to use this material as a protective covering to keep moisture on areas frosted with the "sulfa" drugs. Colebrook and Francis (*Lancet*, March 1, 1941, page 271) found that when a second dressing was done where sulfanilamide was used, all the frosting had dissolved after twenty-four hours; but where sulfathiazole was used some of the material was still undissolved after twenty-four hours, but had all dissolved by forty-eight hours.

In line with the principles of debridement of wounds before using these agents, the use of hydrogen peroxide and other oxidizing agents to remove films of detritus, which would tend to render the drug inert, have been successfully tried. The presence of peptone-like substances from tissue disintegration have a neutralizing effect on the sulfonamide drugs. On the other hand, tissue breakdown is counteracted because the drug keeps down the growth of organisms. Thus, in the case of sulfanilamide, at least, it is possible to get concentrations in the fluids of wounds a hundred times as strong as can be obtained in the blood after therapeutic doses. In addition to the favorable effect of oxidizing agents before the reimplantation of the crystals, we find that chlorine-delivering substances have a particularly helpful effect. At Mare Island Naval Hospital we use the Council-accepted azochloramide, but any other relatively stable chlorine substances would be suitable. An aid in introducing sulfonamide substances into cavities is to apply the crystals to saline-soaked gauze packing, a procedure which could also be carried out in the preparation of skin areas around penetrating and perforating wounds at the time they are first seen.

COMMENT

With the addition of these chemotherapeutic agents to our armamentarium we are enabled to revise our ideas of the treatment of wounds, particularly with regard to the all-important lapsed time factor. As I stated before, common sense and judgment must not be set aside, but certainly we can safely undertake procedures on wounds much later than was formerly thought to be the case. At Mare Island Hospital we treated one patient who had an extensive tendon injury on the dorsum of his forearm. For various reasons, treatment was

delayed for a period of about eighteen hours. Ordinarily no effort would have been made to do a tendon repair on such a patient, but in this case, with the liberal use of a fifty-fifty mixture of sulfanilamide and sulfathiazole powder, a complete repair was made with nonabsorbable suture and the wound proceeded to a complete recovery.

Compound fractures have been treated with more than ordinary success under battle conditions by merely excising the necrotic material, irrigating with saline solution, insufflating or otherwise instilling sulfanilamide crystals, packing open with vaseline gauze, immobilizing with plaster if feasible, and transporting to wherever definitive treatment was to be carried out. At Mare Island Naval Hospital we received many such patients on Christmas Day who were so managed after the December 7 attack at Pearl Harbor. It is contemplated that men going into combat will be provided with tablets for oral use, and that first-aid dressing stations everywhere will have ample supplies of the powder for topical use. There is considerable difference of opinion as to the amount of the substance which can be used at one time. In general, it seems that five grams in one wound, and a total of not more than ten grams in all wounds, seem to be a safe rule, although larger amounts have been used successfully. The best results come from a uniform light application to all the surfaces of a wound rather than the presence of large masses of the substance, which act as foreign bodies or are ejected unused. The sulfonamide group of drugs has been used in the treatment of all types of war wounds, bones, soft tissue, and wounds of the abdominal and thoracic viscera, both primarily and secondarily. Dr. Emile Holman, who is chief of the surgery service at the Mare Island Naval Hospital, has removed two foreign bodies embedded in the cardiac muscle, and after the extraction of these slugs we implanted the sulfanilamide sulfathiazole mixture in the cavities thus created.

At the present time* we have employed only sulfanilamide and sulfathiazole in the management of wounds, and have also used them freely in cases which are not traumatic, where we have reason to suspect or particularly fear infection. Sulfadiazine has been employed only in the treatment of burns, using a 3 per cent solution in 8 per cent triethanolamine, as suggested by K. L. Pickerell in the bulletin of the Johns Hopkins Hospital, 69:217 (August, 1941). This seems promising, but our own experiences are as yet quite limited. Sulfapyradine has not been used by us for local administration. There are already many more sulfa compounds in various stages of investigation and, doubtless, more to come, some of which will probably be demonstrated to have superiority in different ways.

It is highly desirable that sulfonamide compounds be sterilized for topical use. Exposure to dry heat for two hours at a temperature of 150 de-

grees Fahrenheit seems to be satisfactory. Transfer from large to smaller packages must be made with sterile precautions.

PEROXIDES

Another group of substances which are finding new and wide application in traumatic surgery are the peroxides. This is particularly true of the peroxides which give off oxygen slowly and continuously under special conditions, such as zinc and benzoyl peroxide. Considerable experience and literature have accumulated on the use of zinc peroxide in wounds where members of the genus *Clostridium* and other anaerobes are likely to be found. A 40 per cent aqueous suspension is applied to the wound surfaces and crevices after debridement, and arrangements made to keep moisture supplied, as this is necessary for the liberation of oxygen. Benzoyl peroxide seems to be particularly effective in the promotion of healing of surface wounds, and has the added advantage of a mild anesthetic effect. It can be used either as powder, a 10 per cent aqueous suspension, or in an ointment base. Both zinc and benzoyl peroxide can be used in combination with sulfonamides, either applied locally or given by one of the other available routes.

CHLORINE-PRODUCING SUBSTANCES

I have already mentioned the chlorine-producing substances in connection with sulfonamide therapy as an adjunct to surgery. Many of you, no doubt, remember the tedious Dakin treatments developed during the last war. We now have more stable and simpler chlorine-delivering substances in common usage. Chloramine-T and dichloramine-T are available under several trade names. At the present time, at Mare Island Naval Hospital, we are using azochloramid, which has been accepted by the Council on Pharmacy and Chemistry of the American Medical Association. It is employed in isotonic buffered saline solution of 1:3300, which we use for irrigating wounds, and 1:500 in glyceryl triacetate, which we instill into wounds or apply as wet dressings. These dressings are not particularly uncomfortable, and the preparation is stable and definitely effective.

BURN THERAPY

The subject of burn therapy is being covered in other papers presented at this meeting, and it seems best only to mention a few brief points. Tannic acid in its various forms, either alone or in combination with other substances such as silver nitrate, has limited applications, but is unsuitable in general on the face, hands, genitalia, or where there are encircling burns of extremities. Triple dye has its proponents and a special field of usefulness, probably for the most part in conjunction with other materials in certain stages of burn-healing. We received a large number of burns as a result of the Pearl Harbor disaster, but by the time we began their treatment they could be considered more as large open wounds than as burns. They had been treated in various ways at the start. One follow-up treatment which has been employed at Mare Island is the use of a wax and oil spray into which sulfanil-

* May, 1942.

amide, cod-liver oil, menthol, camphor, and eucalyptol have been incorporated. This is kept hot in a water-bath and applied with a spray gun, and the patients kept in the open air without dressing, warmth being provided by cradles and lights. They are allowed to take shower baths and the wax mixture is frequently reapplied.

IRRIGATION SOLUTIONS

Another class of substances is that used for the cleansing of skin and the debridement of wounds. For irrigation in wounds we have used mainly saline solution, although potassium permanganate, in strength varying from 1:2000 to 1:5000, is suitable. We have not employed iodine or the mercuri-cresol preparations, such as merthiolate or metaphen, in wounds involving deep structures, tendons, and bones. Tincture of green soap, either alone or with hydrogen peroxide, is suitable only in the more superficial types of wounds. Skin preparation and cleansing is done usually with mercuri-cresols, and penetrating wounds and compound fracture wounds are lightly plugged, while this is being done to prevent the entrance of these substances into the wound. Where adhesive is to be applied, we usually use merthiolate and then paint the surface with a second coating, using tincture of benzoin.

COMMENT

As has already been stated, the sulfonamides act by inhibiting growth-promoting factors, such as para-aminobenzoic acid. After continued use this may also inhibit cellular growth in the tissue of the animal being treated. Several investigators have found that this can be overcome to a great extent by the application of substances such as allantoin, or 50 per cent urea solution, or benzyl peroxide. Allantoin can be incorporated in an ointment base in 2 per cent strength, along with benzoyl peroxide 10 per cent strength. The use of cod-liver oil also counteracts the tendency to depress the growth of cells.

Perhaps one should not leave the subject of sulfonamide drugs without mentioning toxic reactions, especially since our topical administration is usually augmented by giving the drug orally, intravenously, subcutaneously, or occasionally rectally. We have had numerous cases where a diffuse (often a scarletiform) rash appears. In only one case, however, did we have the rash where the drug was not used in any other manner than locally. We have had several cases which, after the subsidence of fever, developed a high elevation of temperature, and others where there was a diminished urinary output with red blood cells and crystals. We immediately stopped the drug in such cases, and saw no further ill effects. There has been a very small number of cases where the ability to form white cells has been impaired in the group which we have treated.

SUMMARY

Since the last world war many new chemotherapeutic agents have come into use as adjuncts to surgery in treating traumatic wounds. Most notable among these are the sulfonamides, where,

with local application, we can obtain high concentrations at the site where they will be expected to accomplish the most good. This can be made a generalized feature of first-aid under combat conditions to reduce the danger of infection until definitive treatment can be instituted. The stable peroxides offer a weapon to combat anerobic infection, and the more stable chloramine substances provide a readily available means of keeping down wound infection by the liberation of chlorine.

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LARGE VESICAL CALCULUS IN ASSOCIATION WITH GIGANTISM

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THE case here reported is of interest because of the large size of the bladder calculus and because of its occurrence in a patient afflicted with gigantism. The latter is of speculative etiological interest.

REPORT OF CASE

The patient, T. C., a 33-year-old caucasian male laborer, entered the hospital on March 22, 1943, complaining of chills and fever of nine days' duration, with associated urinary frequency and dysuria. He had suffered several similar, although milder, attacks since the first in 1935.

Family History.—Patient's father and mother, who were apparently normal, died of influenza in 1917. There were no siblings.

Past History.—Normal, healthy childhood until the age of eighteen, when he had an osteomyelitis of the left tibia which drained for a year. It was at about this age that the patient began to grow more rapidly than theretofore. Growth continued to the time of admission, his height having increased one-half inch during the past year. Hat, glove, and shoe sizes had increased gradually. Had always